In The Claims

Cancel claims 13-14, 43-44, and 53-54 without prejudice.

Kindly amend claims 1, 7, 9, 27-29, 47-49, and 67-69 as follows:

1. (Currently amended) A medicament delivery method comprising;

(a) providing a delivery system comprising a delivery formulation comprising an effective amount of an inactivated bioactive peptide and an effective amount of a mucosal absorption enhancer comprising a quaternary ammonium salt for enhancing mucosal absorption of the peptide in the buccal cavity;

(b) bringing the delivery formulation into contact with the mucosal surface of the buccal cavity under conditions suitable to permit an effective amount of the peptide to be absorbed, wherein the quaternary ammonium salt is used at a final concentration of about 0.005 % and about 0.05 %, based on the weight of the formulation.

C1

2. (Cancelled)

3. (Previously amended) The method of claim 1 wherein the quaternary ammonium salt comprises benzalkonium chloride.

4. (Original) The method of claim 1 wherein the peptide comprises an ozone-inactivated toxin.

5. (Original) The method of claim 1 wherein the formulation is delivered by spraying to the roof of the mouth.

6. (Original) The method of claim 1 wherein the delivery system further comprises an aerosol actuator, for use in containing and spraying the delivery formulation.

7. (Currently amended) A delivery system comprising a dispenser containing a delivery formulation comprising an effective amount of an inactivated bioactive peptide and an

effective amount of a mucosal absorption enhancer comprising a quaternary ammonium salt for enhancing mucosal absorption of the peptide in the buccal cavity, wherein the quaternary ammonium salt is used at a final concentration of about 0.005 % and about 0.05 %, based on the weight of the formulation.

8. (Previously amended) The system of claim 7 wherein the dispenser is selected from the group consisting of aerosol and non-aerosol dispensers.

9. (Currently amended) A medicament delivery formulation comprising an effective amount of an inactivated bioactive peptide and an effective amount of a mucosal absorption enhancer comprising a quaternary ammonium salt for enhancing mucosal absorption of the peptide in the buccal cavity, wherein the quaternary ammonium salt is used at a final concentration of about 0.005 % and about 0.05 %, based on the weight of the formulation.

C1

10. (Original) A combination comprising a delivery formulation according to claim 9 in contact with the mucosal membrane of the roof of the mouth.

11. (Previously added) The method of claim 1 wherein the peptide has a molecular weight of at least 500 daltons.

12. (Previously added) The method of claim 1 wherein the quaternary ammonium salt comprises a tetrasubstituted ammonium salt, in which the substituent groups comprise hydrocarbon compounds attached to the nitrogen by N-C bonds.

13 (Cancelled)

14. (Cancelled)

15. (Previously added) The method of claim 1 wherein the bioactive peptide is inactivated by a method comprising the steps of treating the peptide with ozone under conditions suitable to oxidize any disulfide bonds in order to form corresponding pairs of cysteic acid

residues, and then stabilizing the resultant cysteic acid residues and preventing the reformation of disulfide bonds.

16. (Previously added) The method of claim 15 wherein the inactivated bioactive peptide retains one or more properties selected from the group consisting of immunogenicity and anti-viral activity.

17. (Previously added) The method of claim 1 wherein the bioactive peptide is selected from the group consisting of toxins affecting the presynaptic neurojunction, toxins affecting the postsynaptic neurojunction, toxins affecting ion channels, and toxins that damage the cell membrane.

18. (Previously added) The method of claim 17 wherein the toxins affecting the presynaptic neurojunction toxins are selected from the group consisting of notexin, ß-bungarotoxin, crotoxin, taipoxin, textilotoxin and α-latrotoxin.

19. (Previously added) The method of claim 17 wherein the toxins affecting the postsynaptic neurojunction are selected from the group consisting of α-conotoxins, α-cobrotoxin, erabutoxin, α-cobratoxin and α-bungarotoxin.

20. (Previously added) The method of claim 17 wherein the toxins affecting ion channels are selected from the group consisting of dendrotoxins, scorpion toxins, m-conotoxins, and sea anemone toxins.

21. (Previously added) The method of claim 17 wherein the toxins that damage the cell membrane are membrane-damaging toxins selected from the group consisting of myotoxins, cardiotoxins, mellitin, and phospholipases.

22. (Previously added) The method of claim 16 wherein the bioactive peptide is selected from the group consisting of protein hormones and enzymes.

23. (Previously added) The method of claim 22 wherein the bioactive peptide is a protein hormone selected from the group consisting of oxytocin, arginine vasopressin, insulin, growth hormone and calcitonin.

24. (Previously added) The method of claim 22 wherein the bioactive peptide is an enzyme selected from the group consisting of ribonuclease, lysozyme, chymotrypsin, trypsin, elastase, and papain.

25. (Previously added) The method of claim 1 wherein the peptide is prepared by a method comprising the step of preparing a cDNA strand encoding the peptide.

26. (Previously added) The method of claim 25 wherein the peptide is prepared by expressing the cDNA under conditions in which the peptide is recovered in an inactive form due to the failure to form one or more disulfide bridges.

27. (Currently amended) A medicament delivery method comprising;

(a) providing a delivery system comprising a delivery formulation comprising an effective amount of an inactivated bioactive macromolecule and an effective amount of a mucosal absorption enhancer comprising a quaternary ammonium salt for enhancing mucosal absorption of the peptide;

(b) bringing the delivery formulation into contact with the mucosal surface under conditions suitable to permit an effective amount of the peptide to be absorbed, wherein the quaternary ammonium salt is used at a final concentration of about 0.005 % and about 0.05 %, based on the weight of the formulation.

28. (Currently amended) The method of claim 27 wherein the bioactive macromolecule comprises a bioactive peptide having a molecular weight of at least 500 daltons, the quaternary ammonium salt comprises benzalkonium chloride ~~at a final concentration of between about 0.001 % and about 0.1 % based on the weight of the formulation~~, the bioactive peptide a) has been inactivated by a method comprising the steps of treating the peptide with ozone under conditions suitable to oxidize any disulfide bonds in order to form corresponding pairs of cysteic acid residues, and then stabilizing the resultant cysteic acid residues and preventing the reformation of disulfide bonds, and b) is selected from the group consisting of toxins affecting the presynaptic neurojunction, toxins affecting the postsynaptic neurojunction, toxins affecting ion channels, and toxins that damage the cell membrane.

29. (Currently amended) The method of claim 28 wherein ~~the benzalkonium chloride is used at a final concentration of about 0.005 % and about 0.05 %, based on the weight of the formulation,~~ the inactivated bioactive peptide retains one or more properties selected from the group consisting of immunogenicity and anti-viral activity, and the bioactive peptide comprises a toxin affecting the postsynaptic neurojunction and is selected from the group consisting of α-conotoxins, α-cobrotoxin, erabutoxin, α-cobratoxin and α-bungarotoxin.

30. (Previously added) The system of claim 7 wherein the quaternary ammonium salt comprises benzalkonium chloride.

31. (Previously added) The system of claim 7 wherein the peptide has a molecular weight of at least 500 daltons.

32. (Previously added) The system of claim 7 wherein the quaternary ammonium salt comprises a tetrasubstituted ammonium salt, in which the substituent groups comprise

hydrocarbon compounds attached to the nitrogen by an N-C bond and are selected from substituted and unsubstituted, saturated and unsaturated, aliphatic and aromatic, branched and normal chain groups.

33. (Previously added) The system of claim 7 wherein the quaternary ammonium salt is used at a final concentration of between about 0.001 % and about 0.1 % based on the weight of the formulation.

34. (Previously added) The system of claim 33 wherein the quaternary ammonium salt is used at a final concentration of about 0.005 % and about 0.05 %, based on the weight of the formulation.

C1 35. (Previously added) The system of claim 7 wherein the bioactive peptide is inactivated by a method comprising the steps of treating the peptide with ozone under conditions suitable to oxidize any disulfide bonds in order to form corresponding pairs of cysteic acid residues, and then stabilizing the resultant cysteic acid residues and preventing the reformation of disulfide bonds.

36. (Previously added) The system of claim 35 wherein the inactivated bioactive peptide retains one or more properties selected from the group consisting of immunogenicity and anti-viral activity.

37. (Previously amended) The system of claim 7 wherein the bioactive peptide is selected from the group consisting of toxins affecting the presynaptic neurojunction, toxins affecting the postsynaptic neurojunction, toxins affecting ion channels, and toxins that damage the cell membrane.

38. (Previously added) The system of claim 37 wherein the toxins affecting the presynaptic neurojunction toxins are selected from the group consisting of notexin, ß-bungarotoxin, crotoxin, taipoxin, textilotoxin and α-latrotoxin.

39. (Previously added) The system of claim 37 wherein the toxins affecting the postsynaptic neurojunction are selected from the group consisting of α-conotoxins, α-cobrotoxin, erabutoxin, α-cobratoxin and α-bungarotoxin.

40. (Previously added) The system of claim 37 wherein the toxins affecting ion channels are selected from the group consisting of dendrotoxins, scorpion toxins, m-conotoxins, and sea anemone toxins.

41. (Previously added) The system of claim 37 wherein the toxins that damage the cell membrane are membrane-damaging toxins selected from the group consisting of myotoxins, cardiotoxins, mellitin, and phospholipases.

42. (Previously added) The system of claim 36 wherein the bioactive peptide is selected from the group consisting of protein hormones and enzymes.

43. (Cancelled)

44. (Cancelled)

45. (Previously added) The system of claim 7 wherein the peptide is prepared by a method comprising the step of preparing a cDNA strand encoding the peptide.

46. (Previously added) The system of claim 45 wherein the peptide is prepared by expressing the cDNA under conditions in which the peptide is recovered in an inactive form due to the failure to form one or more disulfide bridges.

42 47. (Currently amended) A delivery system comprising a dispenser containing a delivery system containing a delivery formulation comprising an effective amount of an inactivated bioactive macromolecule and an effective amount of a mucosal absorption enhancer comprising a quaternary ammonium salt for enhancing mucosal absorption of the peptide, wherein the quaternary ammonium salt is used at a final concentration of about 0.005 % and about 0.05 %, based on the weight of the formulation.

48. (Currently amended) The system of claim 47 wherein the bioactive macromolecule comprises a bioactive peptide having a molecular weight of at least 500 daltons, the quaternary ammonium salt comprises benzalkonium chloride ~~at a final concentration of between about 0.001 % and about 0.1 % based on the weight of the formulation~~, the bioactive peptide a) has been inactivated by a method comprising the steps of treating the peptide with ozone under conditions suitable to oxidize any disulfide bonds in order to form corresponding pairs of cysteic acid residues, and then stabilizing the resultant cysteic acid residues and preventing the reformation of disulfide bonds, and b) is selected from the group consisting of toxins affecting the presynaptic neurojunction, toxins affecting the postsynaptic neurojunction, toxins affecting ion channels, and toxins that damage the cell membrane.

C1

49. (Currently amended) The system of claim 48 wherein ~~the benzalkonium chloride is used at a final concentration of about 0.005 % and about 0.05 %, based on the weight of the formulation,~~ the inactivated bioactive peptide retains one or more properties selected from the group consisting of immunogenicity and anti-viral activity, and the bioactive peptide comprises a toxin affecting the postsynaptic neurojunction and is selected from the group consisting of α-conotoxins, α-cobrotoxin, erabutoxin, α-cobratoxin and α-bungarotoxin.

50. (Previously added) The formulation of claim 9 wherein the quaternary ammonium salt comprises benzalkonium chloride.

51. (Previously added) The formulation of claim 9 wherein the formulation is adapted to be delivered by spraying to the roof of the mouth.

52. (Previously added) The formulation of claim 9 wherein the quaternary ammonium salt comprises a tetrasubstituted ammonium salt, in which the substituent groups comprise hydrocarbon compounds attached to the nitrogen by an N-C bond and are selected from substituted and unsubstituted, saturated and unsaturated, aliphatic and aromatic, branched and normal chain groups.

53. (Cancelled)

54. (Cancelled)

55. (Previously added) The formulation of claim 9 wherein the bioactive peptide is inactivated by a method comprising the steps of treating the peptide with ozone under conditions suitable to oxidize any disulfide bonds in order to form corresponding pairs of cysteic acid residues, and then stabilizing the resultant cysteic acid residues and preventing the reformation of disulfide bonds.

56. (Previously added) The formulation of claim 55 wherein the inactivated bioactive peptide retains one or more properties selected from the group consisting of immunogenicity and anti-viral activity.

57. (Previously amended) The formulation of claim 9 wherein the bioactive peptide is selected from the group consisting of toxins affecting the presynaptic neurojunction, toxins affecting the postsynaptic neurojunction, toxins affecting ion channels, and toxins that damage the cell membrane.

58. (Previously added) The formulation of claim 57 wherein the toxins affecting the presynaptic neurojunction toxins are selected from the group consisting of notexin, ß-bungarotoxin, crotoxin, taipoxin, textilotoxin and α-latrotoxin.

59. (Previously added) The formulation of claim 57 wherein the toxins affecting the postsynaptic neurojunction are selected from the group consisting of α-conotoxins, α-cobrotoxin, erabutoxin, α-cobratoxin and α-bungarotoxin.

60. (Previously added) The formulation of claim 57 wherein the toxins affecting ion channels are selected from the group consisting of dendrotoxins, scorpion toxins, m-conotoxins, and sea anemone toxins.

61. (Previously added) The formulation of claim 57 wherein the toxins that damage the cell membrane are membrane-damaging toxins selected from the group consisting of myotoxins, cardiotoxins, mellitin, and phospholipases.

62. (Previously added) The formulation of claim 56 wherein the bioactive peptide is selected from the group consisting of protein hormones and enzymes.

63. (Previously amended) The formulation of claim 62 wherein the bioactive peptide is a protein hormone selected from the group consisting of oxytocin, arginine vasopressin, insulin, growth hormone and calcitonin.

64. (Previously added) The formulation of claim 62 wherein the bioactive peptide is an enzyme selected from the group consisting of ribonuclease, lysozyme, chymotrypsin, trypsin, elastase, and papain.

65. (Previously added) The formulation of claim 9 wherein the peptide is prepared by a method comprising the step of preparing a cDNA strand encoding the peptide.

66. (Previously added) The formulation of claim 65 wherein the peptide is prepared by expressing the cDNA under conditions in which the peptide is recovered in an inactive form due to the failure to form one or more disulfide bridges.

67. (Currently amended) A medicament delivery formulation comprising an effective amount of an inactivated bioactive macromolecule and an effective amount of a mucosal absorption enhancer comprising a quaternary ammonium salt for enhancing mucosal absorption of the peptide, wherein the quaternary ammonium salt is used at a final concentration of about 0.005 % and about 0.05 %, based on the weight of the formulation.

68. (Currently amended) The system of claim 67 wherein the bioactive macromolecule comprises a bioactive peptide having a molecular weight of at least 500 daltons, the quaternary ammonium salt comprises benzalkonium chloride ~~at a final concentration of between about 0.001 % and about 0.1 % based on the weight of the formulation~~, the bioactive peptide a) has been inactivated by a method comprising the steps of treating the peptide with ozone under conditions suitable to oxidize any disulfide bonds in order to form corresponding pairs of cysteic acid residues, and then stabilizing the resultant cysteic acid residues and preventing the reformation of disulfide bonds, and b) is selected from the group consisting of toxins affecting the presynaptic neurojunction, toxins affecting the postsynaptic neurojunction, toxins affecting ion channels, and toxins that damage the cell membrane.

69. (Currently amended) The formulation of claim 68 wherein ~~the benzalkonium chloride is used at a final concentration of about 0.005 % and about 0.05 %, based on the weight of the formulation,~~ the inactivated bioactive peptide retains one or more properties selected from the group consisting of immunogenicity and anti-viral activity, and the bioactive peptide

comprises a toxin affecting the postsynaptic neurojunction and is selected from the group consisting of α-conotoxins, α-cobrotoxin, erabutoxin, α-cobratoxin and α-bungarotoxin.